Chimerix Corporate Presentation

February 29, 2024

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Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks and uncertainties that could cause actual results to differ materially from those projected. Forward-looking statements include those relating to, among other things, the enrollment and timing of data for the Phase 3 ACTION study, the expected results of Phase 3 ACTION study of ONC201 and dose escalation trials of ONC206, our ability to successfully commercialize our current and future product candidates, the potential for royalty and milestone revenue from strategic collaborations, and projections regarding funding and timing of future data readouts. Among the factors and risks that could cause actual results to differ materially from those indicated in the forward-looking statements are risks related to the timing, completion and outcome of the Phase 3 ACTION study of ONC201; risks associated with repeating positive results obtained in prior preclinical or clinical studies in future studies; risks related to the clinical development of ONC206; and additional risks set forth in the Company's filings with the Securities and Exchange Commission. These forward-looking statements represent the Company's judgment as of the date of this release. The Company disclaims, however, any intent or obligation to update these forward-looking statements.

Investment highlights and key catalysts

Ph 3 ACTION study actively enrolling

Significant commercial potential

Corporate capability and financial flexibility

ONC201 Ph 3 trial enrolling - interim OS data expected in 2025, final OS expected in 2026

First-Line H3 K27M-mutant diffuse glioma – The ACTION Study

- ✓ *No approved therapies targeting H3 K27M diffuse glioma, an area of high unmet medical need*
- ✓ *First in class mechanism of action with clinical validation*
- ✓ *Patent protection thru 2037 (potential additional US patent term extension)*

ONC206 in dose escalation

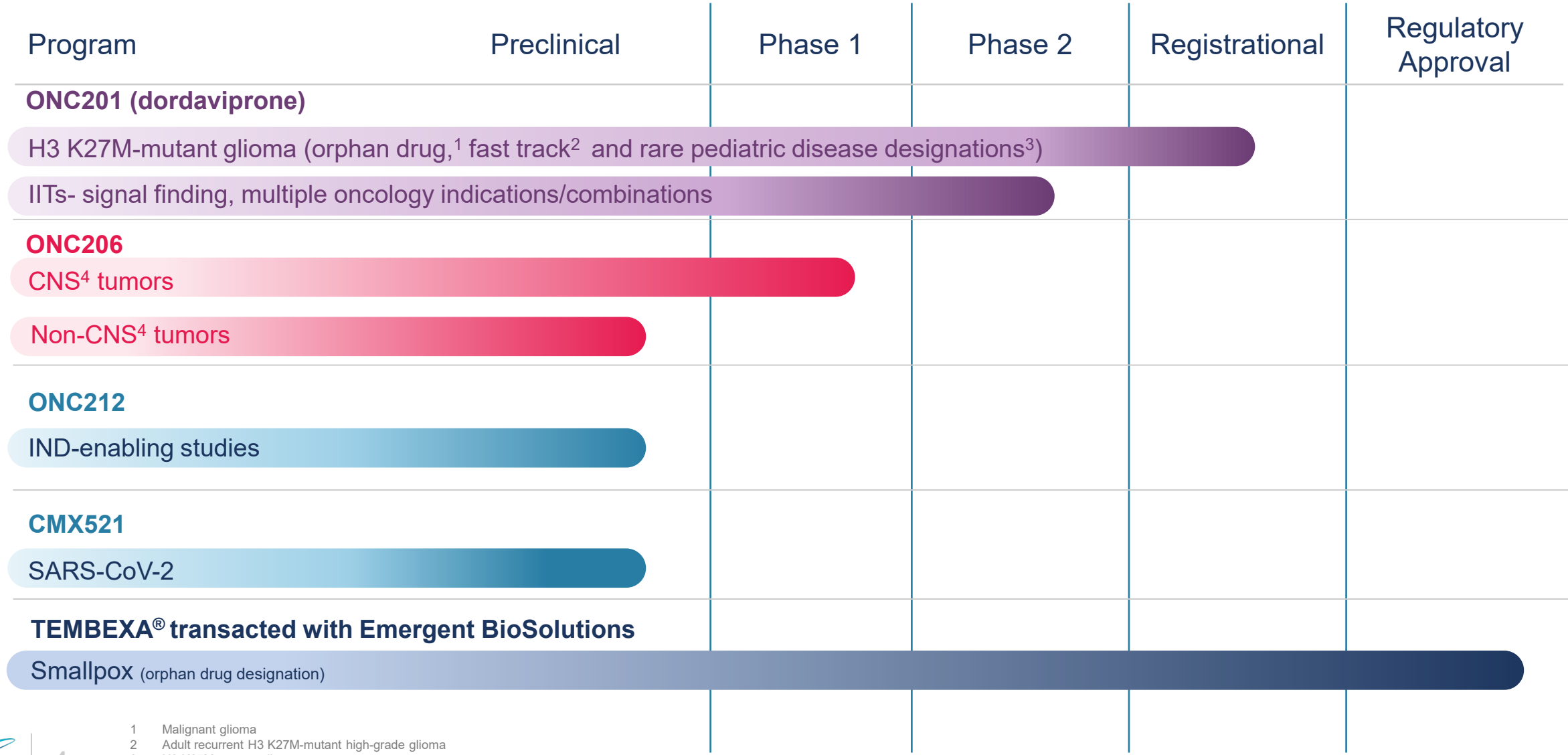
- ✓ *Investigator reported response in non-H3 K27M mutated recurrent glioblastoma patient*
- ✓ *Dose escalation on track for completion beginning in mid 2024*

Early-stage pipeline leverages external capital

- ✓ *Pre-clinical programs potential to advance to clinic or partner (ONC212, CMX521)*
- ✓ *Robust business development search and evaluation process*

$204 million in capital to fund operations as of December 31, 2023, no debt

Deep pipeline across all development stages



1 Malignant glioma
2 Adult recurrent H3 K27M-mutant high-grade glioma
3 H3 K27M-mutant glioma
4. Central Nervous System

ONC201 (dordaviprone) Phase 2 Data Analysis

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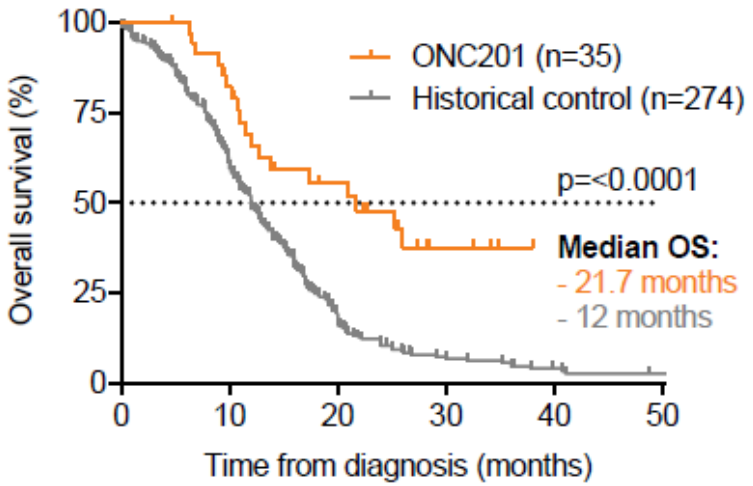
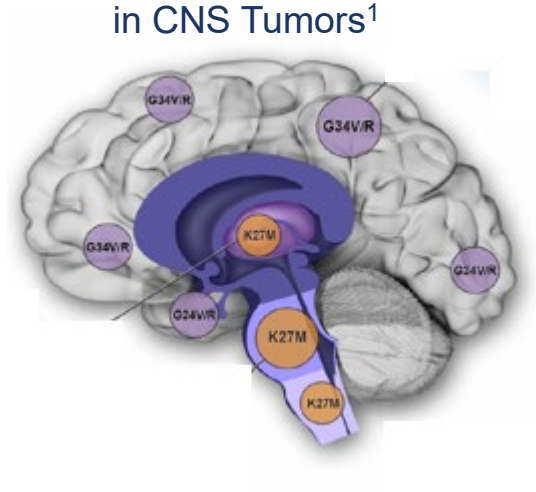
ONC201 data suggests potential to address high unmet need

- H3 K27M mutation is predominantly found among diffuse midline gliomas (DMGs) in young adults and children
- Frontline radiotherapy remains standard of care with transient benefit; resection often not feasible
- DMGs harboring the H3 K27M mutation are WHO Grade IV; historically invariably lethal
- Consistently longer OS of ONC201-treated H3 K27M DMG patients across:
  - Diverse external controls (historical, trials)
  - Sensitivity analysis (early event censoring)
  - Isolated tumor locations (thalamus, brainstem)

Frontline H3 K27M DMG[2]



Histone H3 Mutations in CNS Tumors[1]



Recurrent H3 K27M DMG[3]

	Natural Disease History[4] (n=43)	ONC201 Phase 2 (n=50)
Median OS, mo (95% CI)	5.1 (3.9-7.7)	13.7 (8-20.3)
OS @ 12mo (95% CI)	23.6% (11.7-37.9)	57% (41-70)
OS @ 24mo (95% CI)	11.1% (3.3-24.2)	35% (21-49)

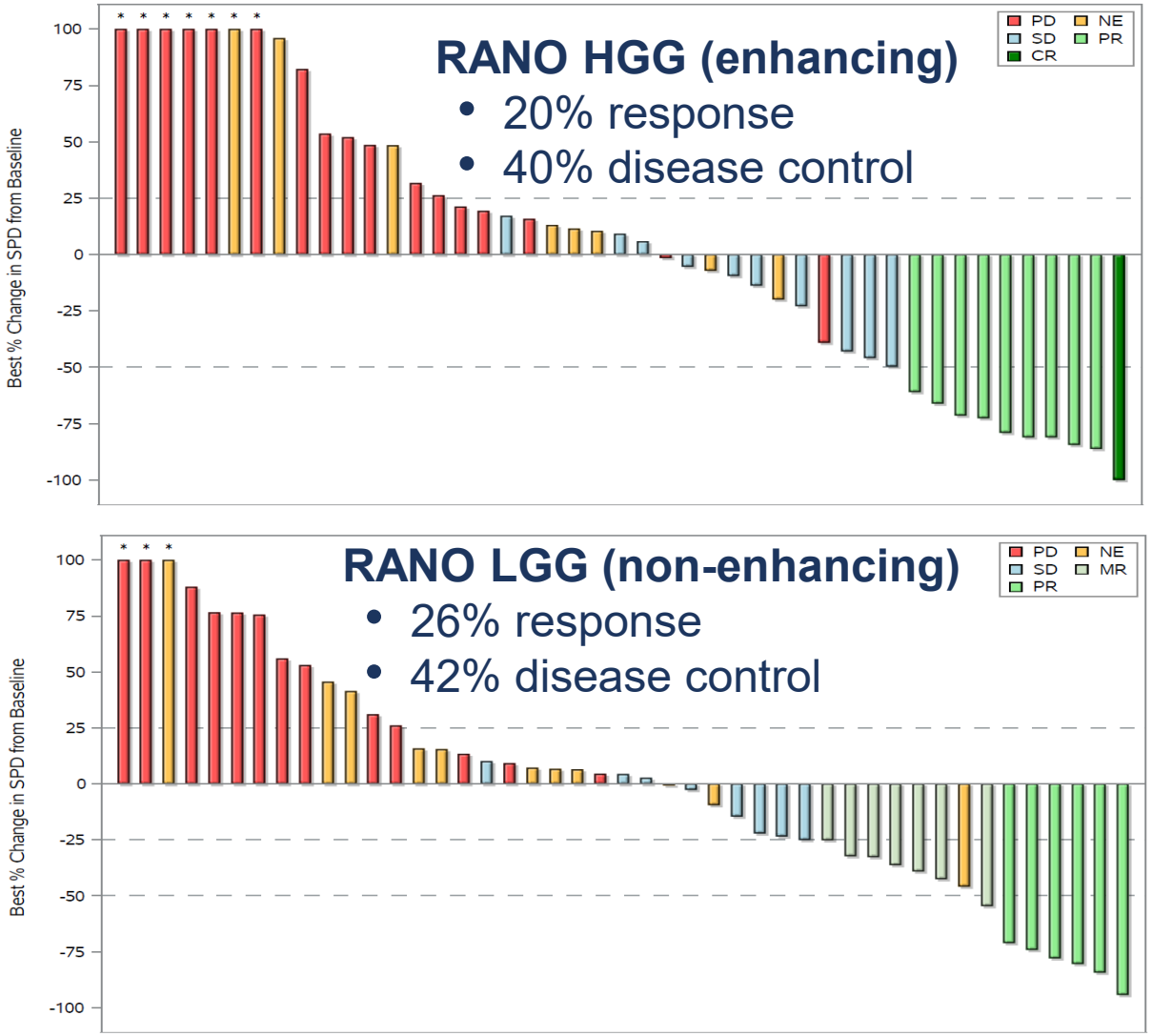
[1] Lulla RR et al. Sci Adv. 2016;2(3):e1501354
[2] Koschmann, Carl et al, "Clinical efficacy of ONC201 in H3 K27M-mutant diffuse midline glioma is driven by disruption of integrated metabolic and epigenetic pathways", Cancer Discovery, Aug 16, 2023
[3] In company sponsored studies
[4] The median OS was 5.1 months for the subset of patients with H3 K27M-mutant diffuse glioma excluding DIPG, CSF dissemination, spinal or leptomeningeal disease (N=12), OS at 12 mos was 25.0%, OS at 24 mos was 16.7%

Phase 2 efficacy for ONC201 in recurrent H3 K27M DMG

- ONC201 monotherapy exhibited durable, clinically meaningful efficacy in recurrent H3 K27M-mutant DMG
  - Overall Response Rate (ORR) of 30% (95% CI: 18 - 45%) by RANO HGG and/or LGG dual reader BICR
  - RANO-HGG criteria assessed by dual reader BICR
    - ORR 20% (95% CI: 10 – 34%)
    - Median Duration of Response (DOR) 11.2 months (95% CI: 3.8 – not reached)
    - Median time to response 8.3 months (range 1.9 – 15.9)
    - Disease control rate 40% (95% CI: 26 – 55%)
    - PFS at 6 months 35% (95% CI: 21 – 49%); PFS at 12 months 30% (95% CI: 17 – 44%)
  - RANO-LGG criteria assessed by dual reader BICR
    - ORR 26% (95% CI: 15 – 40%)
  - Overall survival
    - 12 months: 57% (95% CI:41 – 70%)
    - 24 months: 35% (95% CI: 21 – 49%)
- Improvements observed in performance status and reduction in corticosteroid use
- All Serious Adverse Events considered not related to ONC201 by sponsor

ONC201 waterfall plot – 30% RANO HGG / LGG response

ONC201 Ph 2 Efficacy Analysis by BICR in Recurrent H3 K27M-mutant Diffuse Midline Glioma



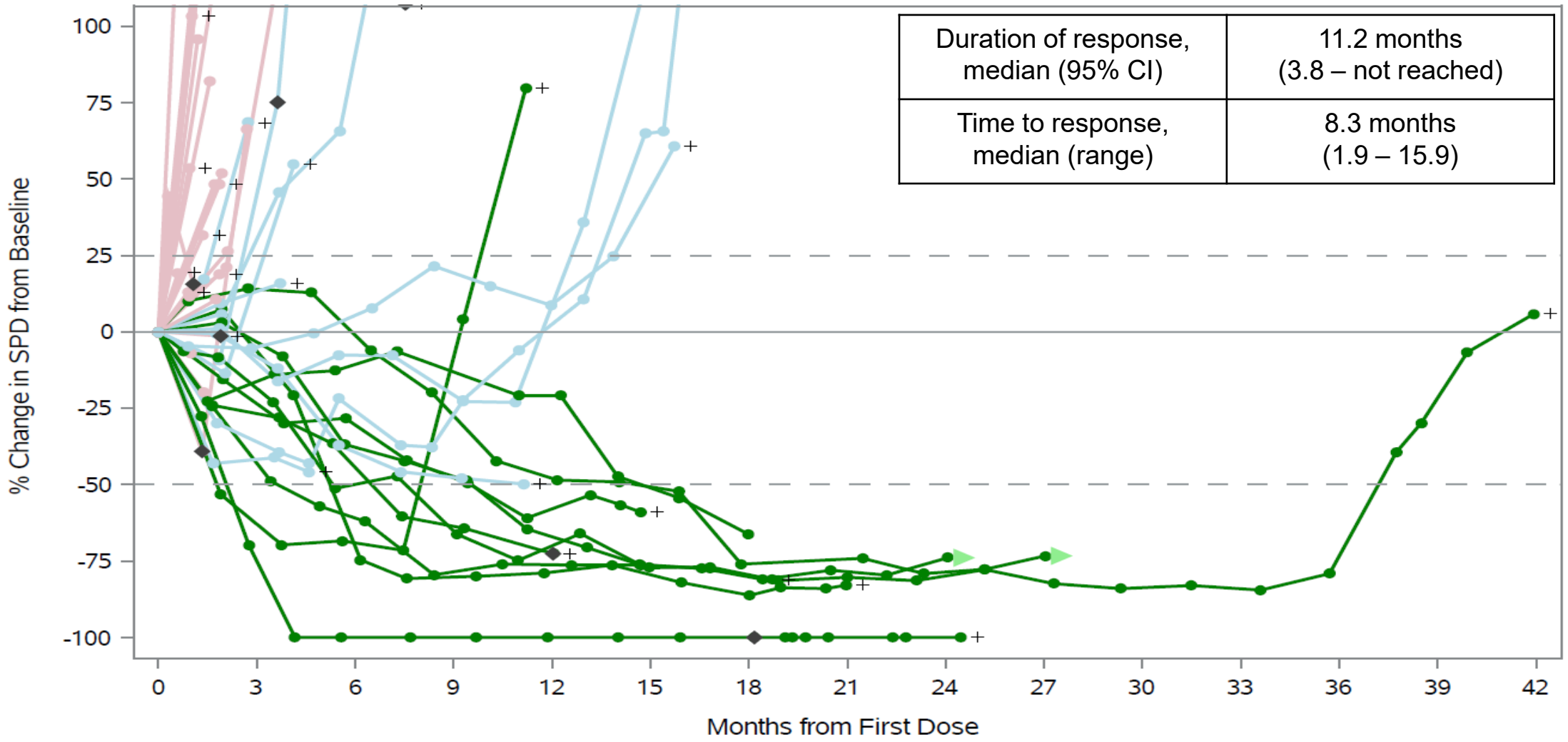
Change > 100%, PR=partial response, MR=minor response, SD=stable disease, NE=not evaluable, PD=progressive disease

- Strict selection criteria to ensure responses attributable to single agent treatment
- Responses require both imaging and clinical criteria
- Dual reader blinded independent central review (BICR)
- Growing consensus that assessment of enhancing and non-enhancing disease (RANO-HGG and RANO-LGG criteria) is needed for diffuse midline glioma

Arrillaga-Romany, et al, Journal of Clinical Oncology, Feb 2024

Clinically meaningful and durable RANO-HGG responses

ONC201 Phase 2 Efficacy Analysis by BICR in Recurrent H3 K27M-mutant Diffuse Midline Glioma



Duration of response, median (95% CI)	11.2 months (3.8 – not reached)
Time to response, median (range)	8.3 months (1.9 – 15.9)

SPD=sum of products of perpendicular diameters (target enhancing lesions per BICR)
Only patients with measurable target enhancing lesions by BICR at baseline and with post-baseline evaluations are included.
Three patients did not have on-treatment monotherapy MRIs available for BICR; one patient censored prior to first on-treatment MRI ; one patient did not have measurable target lesion.

ONC201 safety

Healthy Adult Dose Escalation Study[1] Incidence of ONC201-Related Adverse Events (AE)

	125 mg N=33	375 mg N=15	625 mg N=45
Any treatment-related AE	36.0%	20.0%	51.0%
Grade 1	36.0%	20.0%	51.0%
Grade 2	0	0	0
Grade 3-5	0	0	0

- Treatment-related AEs were generally Grade 1 and transient across the clinical pharmacology program.

Treatment-related Adverse Events in > 5% Glioma Patients

Treatment-related Adverse Events, Integrated Safety Data Set, (N=422 glioma patients) [1]	Related TEAEs	
	All grades	Grade ≥ 3
Any Treatment-related AE	56.2%	11.6%
Fatigue	20.1%	2.1%
Nausea	15.4%	0
Vomiting	11.1%	0.9%
Lymphocyte count decreased	9.2%	1.9%
ALT increased	8.5%	1.4%
Headache	7.3%	0
White blood cell count decreased	7.1%	0.2%
Decreased appetite	5.7%	0
Hypophosphataemia	5.2%	0

1. Based on available data from October 2023 Investigator brochure

ONC201 Phase 3 ACTION Study Summary

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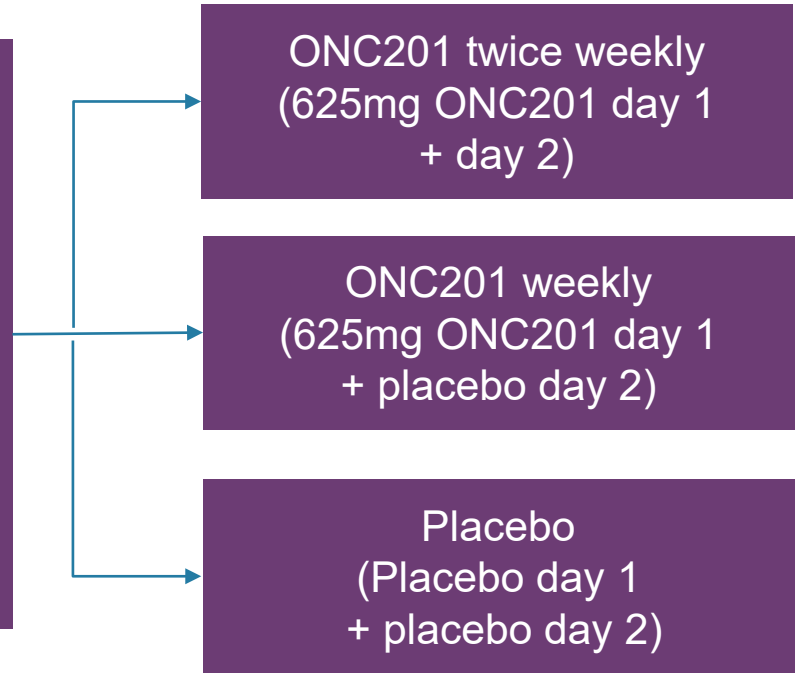
Pivotal Phase 3 ACTION trial design

Now enrolling, a randomized, double-blind, placebo-controlled, multicenter international study in 450 newly diagnosed diffuse glioma patients whose tumor harbors an H3 K27M-mutation.

Key Patient Inclusion

- H3 K27M-mutant diffuse glioma[1]
- Radiation therapy recently completed
- KPS ≥ 70 at time of randomization
- Stable steroid dose
- No prior bevacizumab
- No temozolomide within three weeks

Treatment



Endpoints

- Primary: Overall Survival
- PFS (alpha-allocated)
- Secondary: steroid response, performance status, QoL, neurologic function

1. Excludes DIPG and spinal tumors

Design provides multiple paths for success

Interim data expected in 2025 and final data in 2026

Independent comparisons for each ONC201 arm versus control will be made at each timepoint.

First OS[1] Interim

- ~164 events
- Success at HR[3]~0.52

PFS by RANO HGG[2]

- ~286 events
- Success at HR~0.68

Second OS Interim

- ~246 events
- Success at HR~0.64

Final OS

- ~327 events
- Success at HR~0.73

Powering assumptions 0.65 expected HR for OS and 0.60 expected HR for PFS

1. Overall Survival (OS)
2. Progression-free survival (PFS). PFS may provide valuable data for regulatory discussions.
3. Hazard Ratio

ONC201 Market Opportunity Assessment

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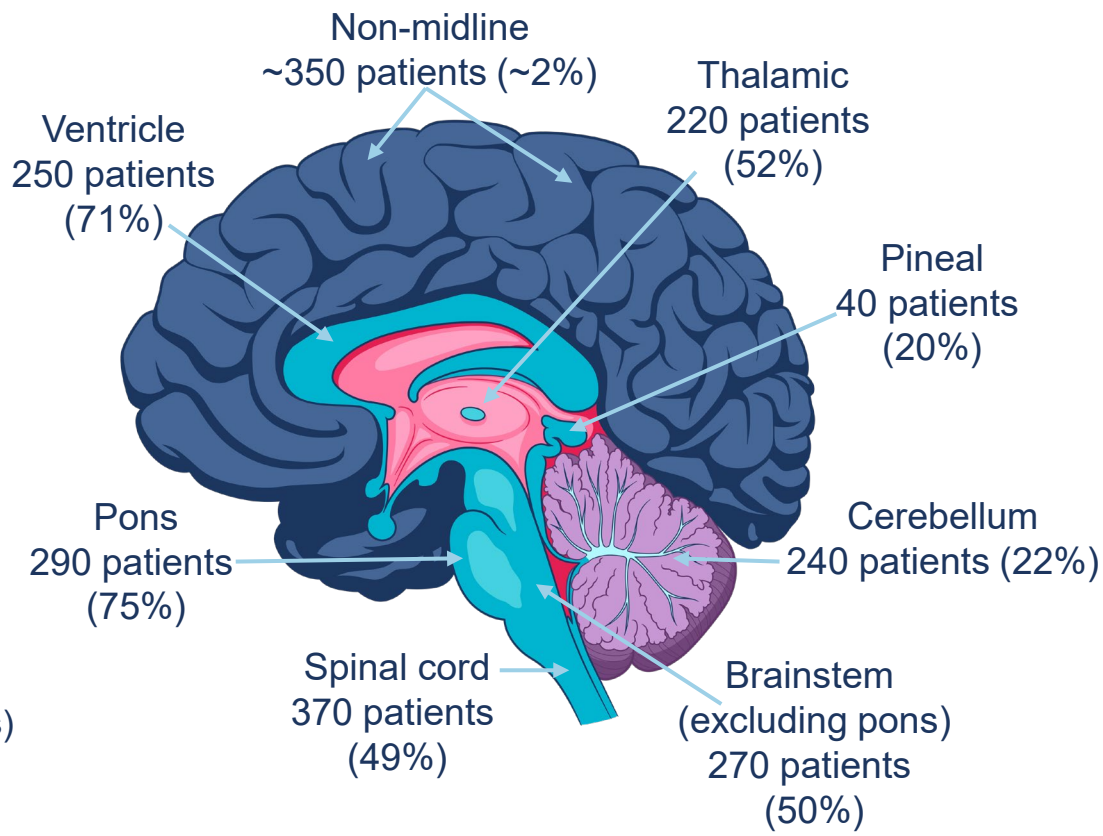
Approximately 21,000 gliomas reported in the U.S. each year, affecting all locations in the brain[1]

- **~40%** of 4,000+ ***midline gliomas*** are expected to harbor the H3 K27M mutation[2]
- **~2%** of 17,000+ ***non-midline gliomas*** are expected to harbor the H3 K27M mutation[2]
- Each year it is estimated that **~2,000** patients are affected by H3 K27M-mutant glioma in the U.S;
  ~5,000 patients in the top seven global markets
  (by extrapolation of the estimated US incidence rate to the top seven markets)
- No approved therapies specifically for H3 K27M mutant glioma

Estimated # of U.S. H3 K27M+ Patients by Tumor Location (rate of positivity)[2]



(1) Ostrom QT, et al. *Neuro Oncol*. 2022;24(Suppl 5):v1-v95; **(2)** Patient numbers and percentages are estimates (weighted avg per sample size) derived from a review of the literature from (2012-2023): (Aihara K, et al. *Neuro Oncol*. 2014;16(1):140-6; Feng J, et al. *Hum Pathol*. 2015;46(11):1626-32; Solomon DA, et al. *Brain Pathol*. 2016;26(5):569-80;Ryall S, et al. *Acta Neuropathol Commun*. 2016;4(1):93; Aboian MS, et al. *AJNR Am J Neuroradiol*. 2017;38(4):795-800; Wang L, et al. *Hum Pathol*. 2018;78:89-96; Castel D, et al. *Acta Neuropathol Commun*. 2018;6(1):117; Karremann M, et al. *Neuro Oncol*. 2018;20(1):123-131; Aboian MS, et al. *AJNR Am J Neuroradiol*. 2019;40(11):1804-1810; Dorfer C, et al. *Acta Neurochir (Wien)*. 2021;163(7):2025-2035; Sievers P, et al. *Neuro Oncol*. 2021;23(1):34-43; Mackay A, et al. *Cancer Cell*. 2017;32(4):520-537 e5; Huang T, et al. *Oncotarget*. 2018;9(98):37112-37124; Schreck KC, et al. *J Neurooncol*. 2019;143(1):87-93; Chiba K, et al. *World Neurosurg*. 2020;134:e530-e539; Mukasa A, et al. *Neuro Oncol*. 2014;16(Suppl 3):iii9-iii10; Castel D, et al. *Acta Neuropathol*. 2015;130(6):815-27; Khuong-Quang DA, et al. *Acta Neuropathol*. 2012;124(3):439-47; Roux A, et al. *Neuro Oncol*. 2020;22(8):1190-1202; Giagnacovo M, et al. *Childs Nerv Syst*. 2020;36(4):697-704; Wu G, et al. *Nat Genet*. 2014;46(5):444-450; Wu G, et al. *Nat Genet*. 2012;44(3):251-3; Taylor KR, et al. *Nat Genet*. 2014;46(5):457-461; Saratsis AM, et al. *Acta Neuropathol*. 2014;127(6):881-95; Erker C, et al. *Neuro Oncol*. 2022;24(1):141-152; Buczkowicz P, et al. *Acta Neuropathol*. 2014;128(4):573-81; Daoud EV, et al. *J Neuropathol Exp Neurol*. 2018;77(4):302-311; Chai RC, et al. *Acta Neuropathol Commun*. 2020;8(1):40; Yi S, et al. *Neurosurgery*. 2019;84(5):1072-1081; Gessi M, et al. *Acta Neuropathol*. 2015;130(3):435-7; Alvi MA, et al. *Mod Pathol*. 2019;32(9):1236-1243; Crotty EE, et al. *J Neurooncol*. 2020;148(3):607-617; Dono A, et al. *J Clin Neurosci*. 2020;82(Pt A):1-8; Akinduro OO, et al. *J Neurosurg Spine*. 2021;35(6):834-843; Nakata S, et al. *Brain Tumor Pathol*. 2017;34(3):113-119; Nomura M, et al. *Acta Neuropathol*. 2017;134(6):941-956; Eschbacher KL, et al. *Am J Surg Pathol*. 2021;45(8):1082-1090; D'Amico RS, et al. *J Neurooncol*. 2018;140(1):63-73; Korshunov A, et al. *Acta Neuropathol*. 2015;129(5):669-78; Aibaidula A, et al. *Neuro Oncol*. 2017;19(10):1327-1337.)

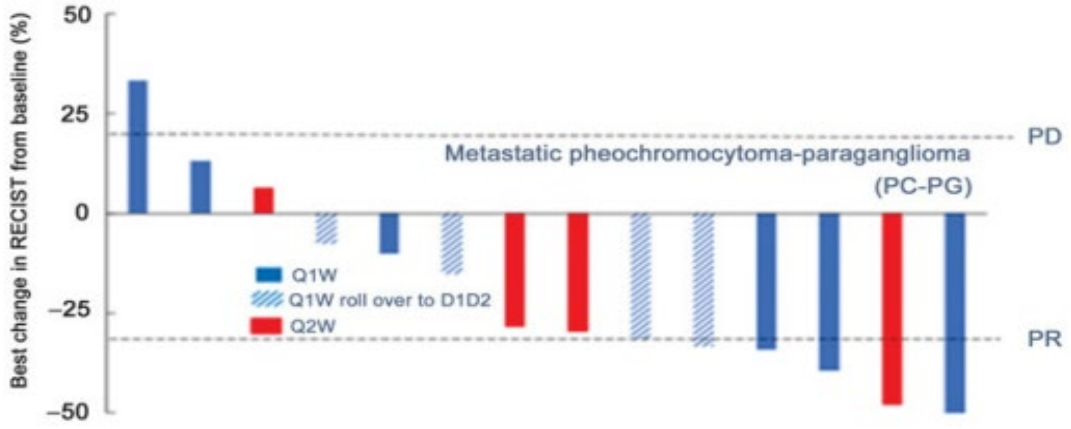
H3 K27M-mutant glioma: rapid ramp to peak revenue expected

- No approved therapies for H3 K27M mutant glioma, ONC201 is the leading program targeting this mutation globally
- Potential market opportunity ~$750 million
- Approximately 5,000 patients in top seven markets[1]
- Ultra-orphan indication drug pricing
- H3 K27M mutations most often in children / young adults
- Low barriers to adoption
  - No effective alternative therapies
  - High unaided awareness among neuro-oncologists
  - Mutation routinely identified by existing diagnostics
  - Longer-term, potentially combinable with other glioma therapies
- Patent protection for lead indication into 2037 - potential U.S. patent term extension (up to five years)

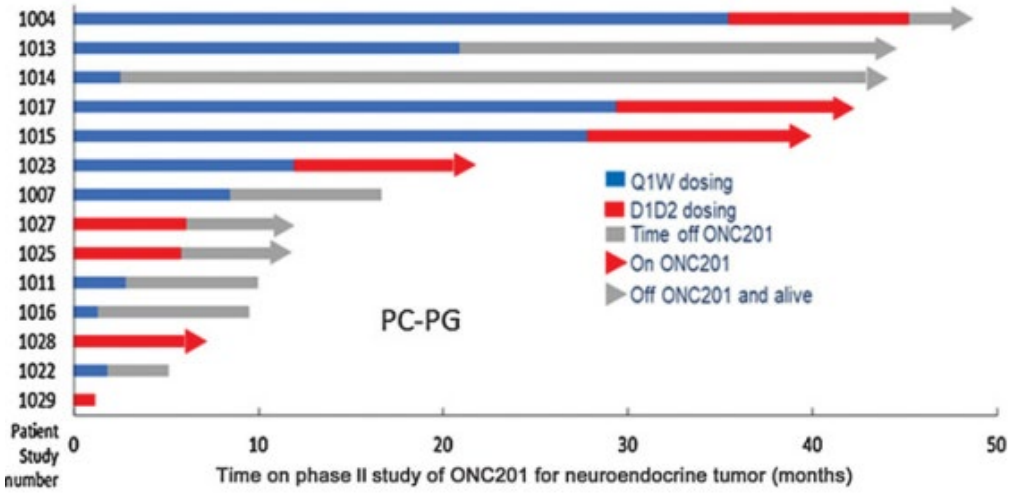
1. By extrapolation of the estimated US incidence rate to the top seven markets

Potential for ONC201 beyond brain tumors

ONC201 efficacy results in dopamine-secreting tumors outside the brain



Ph 2 Study of ONC201 in Neuroendocrine Tumors in investigator-reported data from clinical trial NCT # (NT03034200)



- Single agent responses in Ph 2 neuroendocrine trial of ONC201 observed in subset (PCPG)
- PCPG are adrenal-related tumors with elevated DRD2 expression
- Five patients have been treated > 1 year
- Fewer short-term and potential long-term toxicities than other paraganglioma therapies

1. https://aacrjournals.org/clincancerres/article/28/9/1773/694456/Phase-II-Study-of-ONC201-in-Neuroendocrine-Tumors

ONC201 Mechanism of Action

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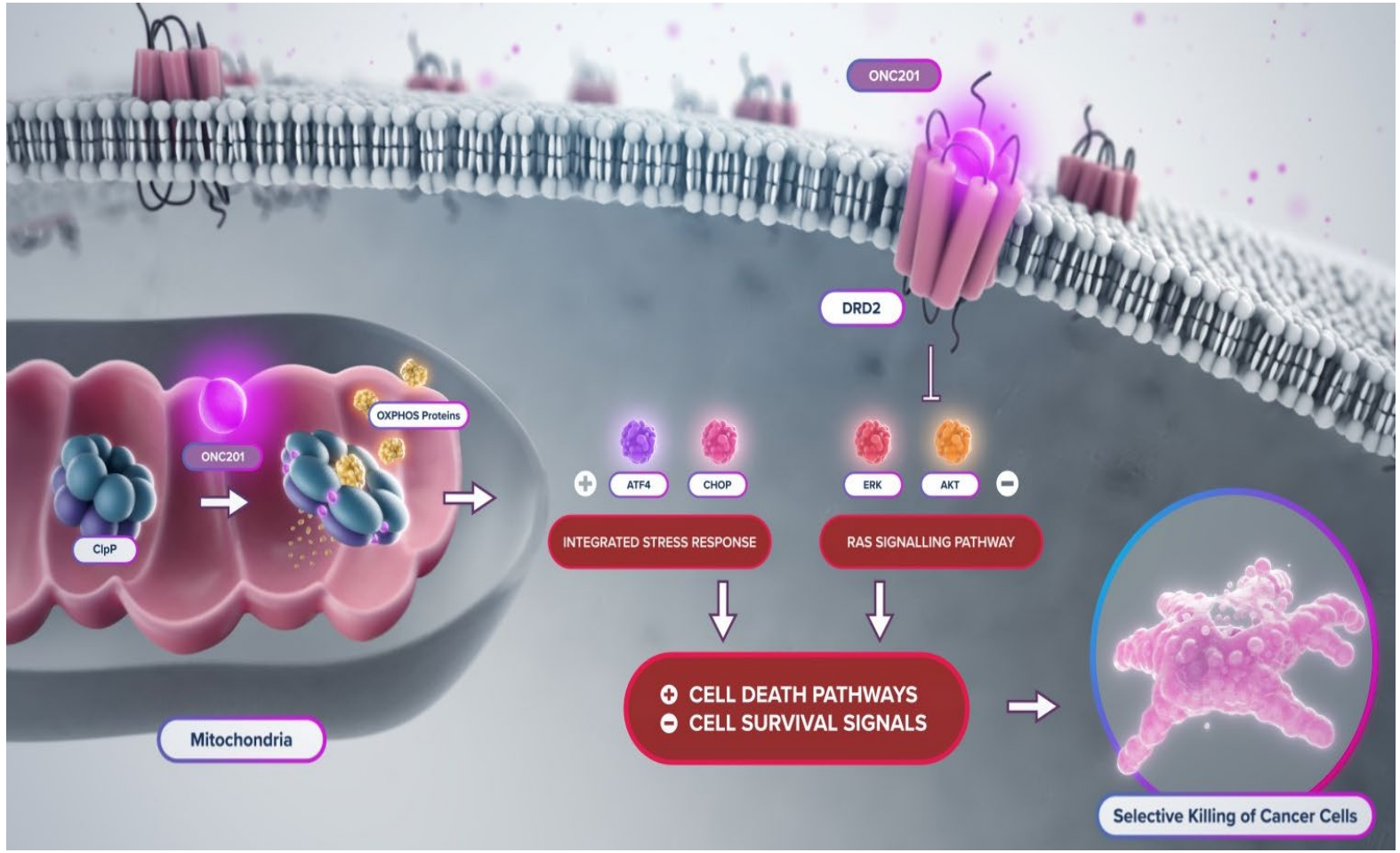
ONC201 directly engages DRD2 and ClpP

ONC201 upregulates integrated stress response, inactivates Akt/ERK, and selectively induces tumor cell death



- ONC201 can selectively induce apoptosis in cancer cells by altering the activity of two protein targets
- DRD2 antagonism
  - DRD2 is a G protein-coupled neuroreceptor that regulates Ras signaling
  - ONC201 antagonizes DRD2, inhibiting Ras signaling pathways
- ClpP agonism
  - ClpP normally degrades misfolded proteins in mitochondria
  - ONC201 modifies ClpP conformation, promoting excess degradation of specific mitochondrial proteins important for cancer cell viability

ClpP=caseinolytic protease P; OXPHOS=oxidative phosphorylation; DRD2=Dopamine receptor D2; ATF4=activating transcription factor 4; CHOP=C/EBP-homologous protein; ERK=extracellular-regulated kinase;

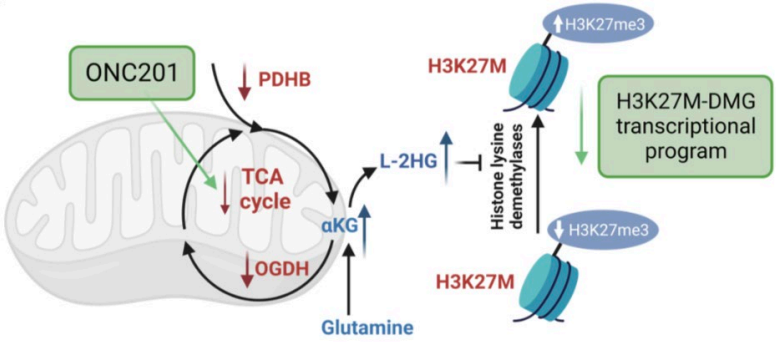
Mechanism and frontline clinical efficacy in H3 K27M DMG

CANCER DISCOVERY

RESEARCH ARTICLE | AUGUST 16 2023

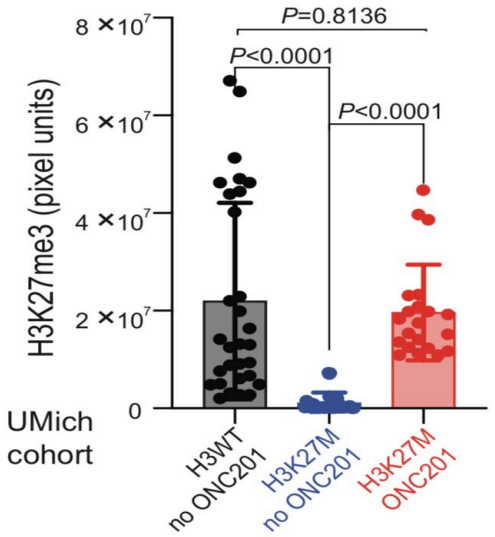
Clinical efficacy of ONC201 in H3K27M-mutant diffuse midline gliomas is driven by disruption of integrated metabolic and epigenetic pathways

Mitochondrial effects reverse H3 K27me3-loss hallmark of H3 K27M



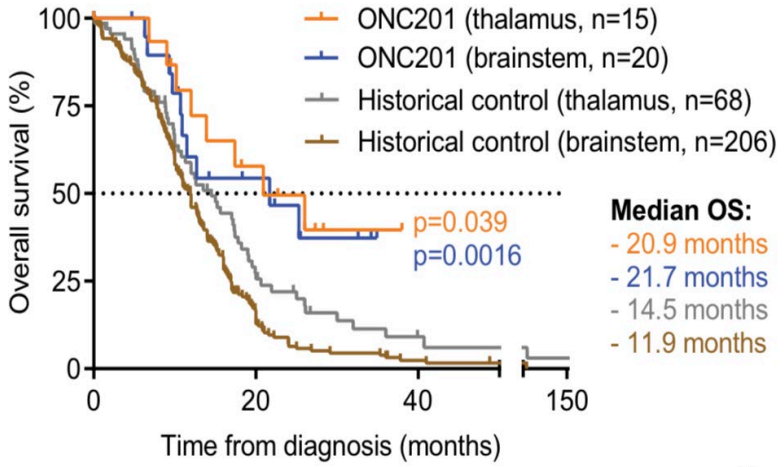
Provides ClpP connection to H3 K27M
Anchors MOA directly to targeting H3 K27M

H3 K27me3-loss reversal evident in ONC201-treated H3 K27M patients



Increased confidence in Ph3 dose

Front-line ONC201 following RT survival benefit



Extends documented benefit to front-line, pediatrics, and brainstem

ONC206

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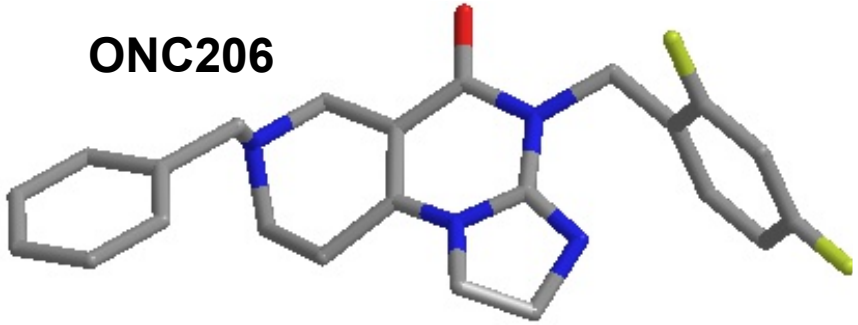
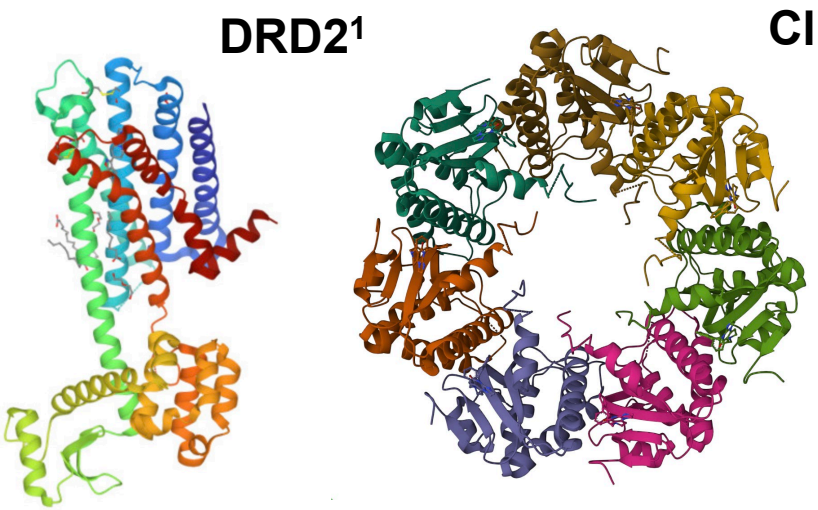
ONC206: oral brain penetrant DRD2 antagonist + ClpP agonist

- Second generation imipridone
  - Increased potency
  - Indications beyond H3 K27M-mutant glioma
- Monotherapy efficacy across multiple preclinical models of CNS and non-CNS tumors
  - Tumor regression in patient-derived xenografts
- Oral dose escalation trials with intensified dosing are ongoing in CNS cancers
- Monotherapy response in recurrent GBM patient without the H3 K27M mutation
  - Differentiated from ONC201 glioma responses that were exclusive to H3 K27M





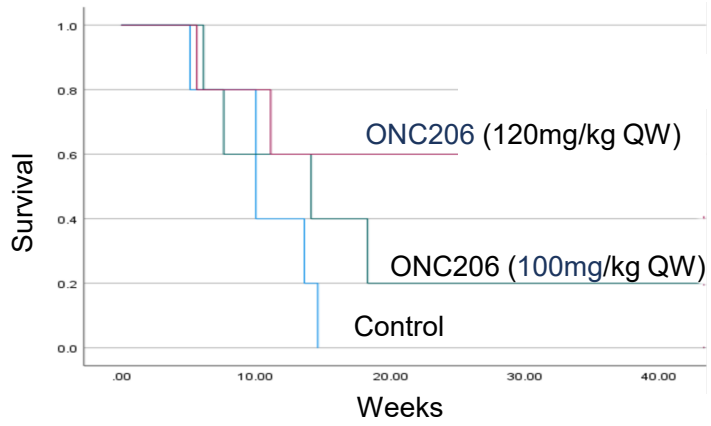
1. PDB 6CM4
2. PDB 6DL7

ONC206 monotherapy activity CNS and non-CNS cancer models

CNS Tumors

Glioblastoma[1]

Medulloblastoma[2]



Transgenic Medulloblastoma Model[2]

Non-CNS Solid Tumors

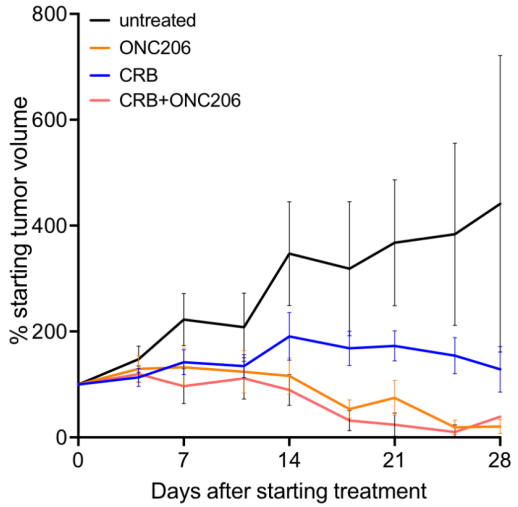
Cholangiocarcinoma[1]

Endometrial cancer[3]

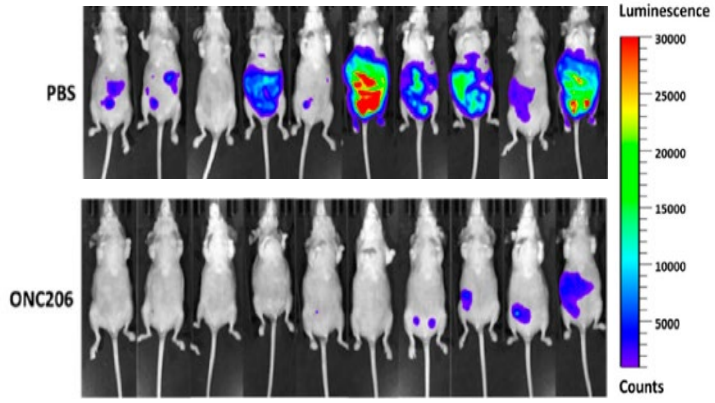
Pheochromocytoma/paraganglioma

Ovarian cancer[4]

Triple-negative breast cancer[5]



BCM2665 Human TNBC PDX (ONC206 100mg/kg BW; Carboplatin - CRB 50mg/kg QW)[5]



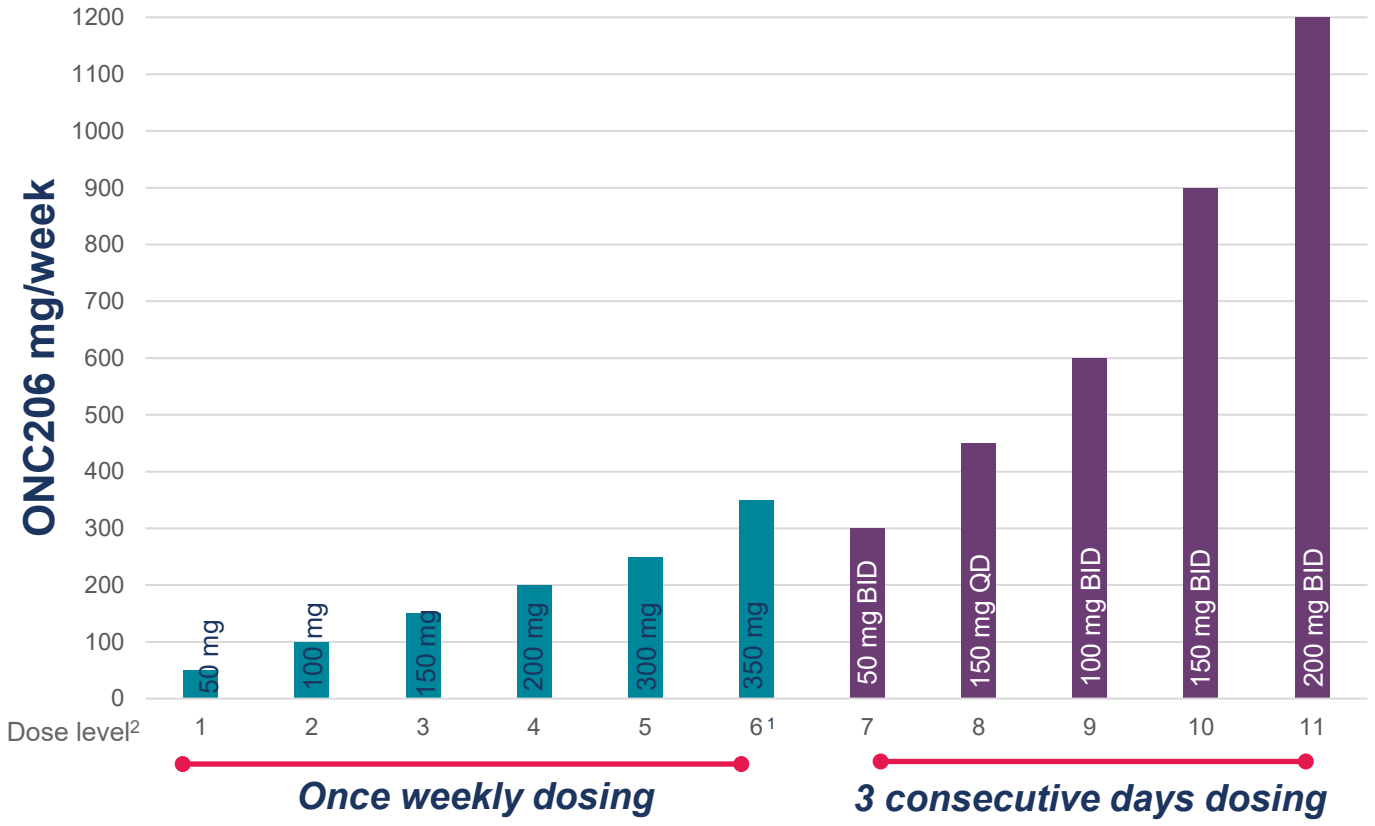
ARK1 Human Endometrial Cancer Xenograft (100mg/kg BW; 6 wks)[3]

1. Theeler et al, SNO 2020
2. Malhotra et al, ISPNO 2020
3. Hu et al, Cancers 2020
4. Tucker et al, American Journal of Cancer Research, 2022
5. Baek et al, SABCS 2023

ONC206 dose escalation to more frequent dosing ongoing

Dose escalation on track for completion in mid 2024

- No DLTs observed with weekly dosing[3]
  - Similar safety profile in adults and pediatrics
  - Majority of treatment-related AEs are mild to moderate
  - Most common treatment-related events are fatigue, lymphocyte count decreased, and vomiting
  - No dose related toxicity with dose escalation[3] – dose escalation continuing



1. Dose level 6 was conducted in adults only
2. Pediatric dose scaled by body weight
3. As of publication date February 29, 2024

Ongoing pipeline development

- ONC212 GPR132 + ClpP agonist
  - GLP-tox studies complete, potential to advance to IND, work performed with support from acedemic grants
  - Preclinical studies are ongoing to evaluate additional oncology indications and predictive biomarkers for ONC212 for clinical development
- CMX521 anti-SARS-CoV-2 preclinical activity
  - Monotherapy efficacy in mouse-adapted SARS-CoV-2-MA10 model across multiple endpoints
  - $2m grant to fund research collaboration with University of North Carolina/READDI[1]

1. Rapidly Emerging Antiviral Drug Development Initiative

Corporate Update

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TEMBEXA® deal term summary

Emergent BioSolutions is an experienced biodefense company collaborating with government agencies to protect public health

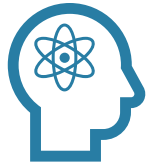
Terms summary:

- $238 million received upfront at closing in Q3 2022
- Up to an additional $124 million in potential BARDA procurement milestones
- 20% royalty on future U.S. gross profit with volumes above 1.7 million courses of therapy
- 15% royalty of all international gross profit
- Up to an additional $12.5 million in development milestones

TEMBEXA®
brincidofovir
10 mg/mL oral suspension | 100 mg tablets

Financial strength supports development through key catalysts

Ph 3 ACTION study actively enrolling



Significant commercial potential

Corporate capability and financial flexibility

ONC201 Ph 3 trial enrolling - interim OS data expected in 2025, final OS expected in 2026

First-Line H3 K27M-mutant diffuse glioma – The ACTION Study

- ✓ *No approved therapies targeting H3 K27M diffuse glioma, an area of high unmet medical need*
- ✓ *First in class mechanism of action with clinical validation*
- ✓ *Patent protection thru 2037 (potential additional US patent term extension)*

ONC206 in dose escalation

- ✓ *Investigator reported response in non-H3 K27M mutated recurrent glioblastoma patient*
- ✓ *Dose escalation on track for completion beginning in mid 2024*

Early-stage pipeline leverages external capital

- ✓ *Pre-clinical programs potential to advance to clinic or partner (ONC212, CMX521)*
- ✓ *Robust business development search and evaluation process*

$204 million in capital to fund operations as of December 31, 2023, no debt

Chimerix Corporate Presentation

CHIMERIX